UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

July 1, 2002

MEMORANDUM:

SUBJECT: **Dimethoate** (035001): Dietary exposure estimates for dimethoate residues of concern in meat, milk, poultry, and eggs.
DP Barcode: D283888
Reregistration Case: 0088

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THROUGH: Susan V. Hummel, Branch Senior Scientist
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TO: Diana Locke, Risk Assessor
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The HED Metabolism Assessment Review Committee (MARC) has concluded (D280775, B. Cropp-Kohlligian, 03/20/02) that the tolerance expression and risk assessments for dimethoate should include residues of dimethoate and omethoate. The Committee further concluded that the following cholinesterase-inhibiting metabolites should be included in the dietary (food) risk assessments for dimethoate but not the tolerance expression: O-desmethyl omethoate, O-desmethyl omethoate carboxylic acid, O-desmethyl isodimethoate, hydroxy dimethoate and its conjugate, hydroxy omethoate and its conjugate, N-desmethyl dimethoate, N-desmethyl omethoate, O-desmethyl dimethoate, and dimethoate carboxylic acid. *See Attachment for chemical structures of the compounds named above.*

As required by the MARC, dietary exposure estimates for dimethoate residues of concern in meat, milk, poultry, and eggs are provided herein.

EXECUTIVE SUMMARY

In animals, as in plants, dimethoate is rapidly metabolized by competing hydrolytic and oxidative processes. Evidence, taken in total, does not clearly indicate that omethoate is a major metabolite of dimethoate in mammals.

In the rat (urine), the principal pathway for the metabolism of dimethoate involves cleavage of the C-N bond to yield dimethoate carboxylic acid (29-46% of dose) that is subsequently metabolized to dimethyl dithiophosphate, dimethyl thiophosphoric acid and dimethyl phosphoric acid. A minor metabolic pathway involves oxidation of dimethoate to its oxygen analog, omethoate (1-6% of dose), that is subsequently metabolized to dimethyl thiophosphoric acid and dimethyl phosphoric acid. Loss of the methoxy groups of the parent to yield carbon dioxide is another minor metabolic pathway.

In ruminants and poultry (tissues such as liver, milk, eggs), one pathway for the metabolism of dimethoate involves conversion of dimethoate to its oxygen analog, omethoate (<10% of the TRR in all tissues, milk, and eggs), and cleavage of the P-S bond, resulting in the phosphorylation of natural products. Another involves cleavage of the C-N bond to yield dimethoate carboxylic acid (maximum ca. 16% of the TRR).

Based on available ruminant, poultry, and rat metabolism data, the only dimethoate residues of concern which are likely to be incurred in meat, milk, poultry, and eggs from ingestion of dimethoate by livestock are residues of omethoate (found in liver and egg whites samples) and dimethoate carboxylic acid (found in liver, egg whites, and milk samples). No detectable residues of dimethoate were found in liver, kidney, fat, muscle, milk, and egg samples from the available ruminant and poultry metabolism and feeding studies.

Based on the available residue chemistry data (ruminant and poultry metabolism and feeding studies), detectable dimethoate residues of concern are not likely to be incurred in meat, fat, and kidney of livestock (ruminants and poultry) resulting from the maximum theoretical dietary burdens to livestock. Dietary exposure estimates for dimethoate residues of concern in meat, fat, and kidney of livestock (ruminant and poultry) should be estimated at zero.

Below are dietary exposure estimates for dimethoate residues of concern (parent, omethoate, and dimethoate carboxylic acid) in liver, milk, and eggs resulting from the maximum theoretical dietary burdens to livestock.

Table 1. Dietary exposure estimates for dimethoate residues of concern in liver, milk, and eggs resulting from the maximum theoretical dietary burdens to livestock. Note: Estimates are the highest levels calculated from either the available metabolism or feeding studies.

Commodity	Dimethoate (ppm)	Omethoate (ppm)	Dimethoate carboxylic acid (ppm)
Liver, ruminants	zero	0.02	0.006
Liver, poultry	zero	0.004	0.007
Milk	zero	0.02	0.004
Eggs	zero	<0.01	<0.001

The following are noted as dimethoate data deficiencies/uncertainties which could lead to underestimations of dimethoate residues of concern in meat, milk, poultry, and eggs:

- Storage stability data to support the feeding study data are not available
- Test sample storage information for the ruminant feeding study is not available
- Magnitude of the residue data for cotton gin byproducts, which is potentially a significant contributor to the ruminant dietary burden, are not available

DETAILED CONSIDERATIONS

A. Maximum Theoretical Dietary Burden Calculation for Livestock

Table 2. Calculation of maximum theoretical dietary burdens for dimethoate.

Feed Commodity	Reassessed Tolerance (ppm)	% Dry Matter	% of Diet	Burden (ppm)
Beef cattle				
Alfalfa, forage	2	35	70	4.00
Dried citrus pulp	5	91	20	1.10
Corn, field, grain	0.1	88	10	0.01
		TOTAL	100	**5.11**
Dairy cattle				
Wheat, forage	2	25	60	4.80
Dried citrus pulp	5	91	20	1.10
Corn, field, grain	0.1	88	10	0.01
		TOTAL	90	**5.91**
Poultry				
Corn, field, grain	0.1	88	80	0.08
Pea, field	2	90	20	0.40
		TOTAL	100	**0.48**

Data Deficiencies/Uncertainties: Residue data are not available for cotton gin byproducts; hence, the beef and dairy maximum dietary burden estimates may be underestimations.

B. Ruminant Residue Chemistry Data

1. [^{14}C-methoxy]dimethoate Metabolism Study

Study Citation: **43583302** Jalali, K.; Krautter, G.; Cassidy, J. (1995) The Metabolism of (^{14}C)-Dimethoate in the Lactating Goat Following Oral Administration for 3 Consecutive Days: Lab Project Number: 760E/411W: 760E/411W-1. Unpublished study prepared by PTRL East, Inc. and PTRL West, Inc. 291 p.

Agency Review of Study: D213956, B. Cropp-Kohlligian, 04/30/96.

Study Summary: Two goats were orally dosed once a day for 3 consecutive days with [^{14}C-methoxy]dimethoate at a dose equivalent to 30.2 ppm in the feed. This dose level represents ca. 5.9x and 5.1x the maximum theoretical dietary burdens for beef and dairy cattle, respectively. Extraction

and protease hydrolysis released ca. 65-90% of the TRR from milk and tissues, with the exception of fat, which was not analyzed owing to a low TRR (<0.05 ppm). Dimethoate *per se* was not detected (<0.01 ppm, <1%TRR) in any tissue or milk sample. HPLC analyses of solubilized residues identified dimethoate carboxylic acid in milk (0.019 ppm, 8.3% TRR) and liver (0.032 ppm, 2.6% TRR), and omethoate in liver (0.120 ppm, 9.8% TRR). However, confirmation of these metabolites in milk and tissues by a second method was unsuccessful due to matrix interferences. The identity of dimethoate carboxylic acid was confirmed in urine. Additional HPLC analyses of benzyl-derivatized ^{14}C-residues indicated that 2-6% of the TRR in milk, muscle, and liver, and 13.4% of the TRR in kidney consisted of simple anionic metabolites such as dimethyl thiophosphate and dimethyl phosphate, which were identified as major metabolites in urine.

Additional characterization and identification of ^{14}C-residues in milk is required. Polar residues extracted with acetonitrile:water accounting for 57% of the TRR should be hydrolyzed, characterized chromatographically, and identified. In addition, almost half of the TRR (45.2% TRR; 0.103 ppm) isolated in the acidic fractions following anion exchange chromatography of solvent extracted milk residues were not further analyzed. These residues must be further characterized and identified.

Table 3. Summary of maximum dimethoate residues of concern found in tissue and milk samples from the goat metabolism study. Represents ca. 5.9x and 5.1x the maximum theoretical dietary burdens for beef and dairy cattle, respectively.

Commodity	Dimethoate	Omethoate	Dimethoate Carboxylic Acid
Liver	nd	9.8%TRR (0.120 ppm)	2.6%TRR (0.032 ppm)
Kidney	nd	nd	nd
Muscle	nd	nd	nd
Fat	nd	nd	nd
Milk	nd	nd	8.3%TRR (0.019 ppm)

nd = <1%TRR; <0.01 ppm

2. Feeding Study 1 - dimethoate fed

Study Citation: **00077543** Hill, R. (1962) To Develop and Validate the Analytical Method for the Determination of Cattle Tissue: To Determine the Possible Presence of Dimethoate in Tissue of Cattle after Feeding of the Insecticide: Laboratory No. 2G6027. (Unpublished study received Jul 24, 1963 under unknown admin.no.; prepared by Diablo Laboratories, Inc., submitted by American Cyanamid Co., Princeton, N.J.; Cdl:222319-G)

Agency Review of Study: Residue Chemistry Chapter of the Dimethoate Registration Standard dated 09/30/82

Study Summary: Dimethoate was not detected (<0.05 ppm) in liver, kidney, heart, muscle, and fat of Holstein calves slaughtered after 14 days of oral administration of 0.5 or 1.0 mg dimethoate per kg body weight (approximately 9 and 18 ppm in the diet). Omethoate was not determined by the residue method used in this study.

2. Feeding Study 2 - dimethoate and omethoate fed

Study Citation: **00073444** American Cyanamid Company (1967) Report of Residue Analysis: PCB-67-4. (Compilation of reports by U.S. agricultural Research Service, Entomology Research Div., Pesticide Chemicals Research Branch, Analytical Investigations; unpublished study, including PCB-67-8;CDL:091160-F)

Agency Review of Study: Residue Chemistry Chapter of the Dimethoate Registration Standard dated 09/30/82

Study Summary: Residues of dimethoate and omethoate were not detected (<0.01 ppm each compound) in liver, kidney, muscle, and fat of beef cattle fed 0.3 mg dimethoate and 0.03 mg omethoate per kg body weight (a dietary level of approximately 6-10 ppm; ca. 1-1.7x the maximum theoretical dietary burden for dairy cattle) for 14 days.

Milk from cows administered capsules containing 0.5 mg dimethoate and 0.05 mg omethoate per kg body weight (approximately dietary level of 10-15 ppm; ca. 1.7-2.5x the maximum theoretical dietary burden for dairy cattle) did not contain detectable residues (<0.01 ppm) of either compound over the 14-day duration of the study. When the study was repeated at twice the dosage (ca. 3.4-5x the maximum theoretical dietary burden for dairy cattle), omethoate was detected in all milk samples at levels up to 0.125 and 0.117 ppm. Dimethoate *per se* was not detected at the higher dose.

C. Poultry Residue Chemistry Data

1. [^{14}C-methoxy]dimethoate Metabolism Study

Study Citation: **43583301** Jalali, K.; Krautter, G.; Cassidy, J. (1995) The Metabolism of (^{14}C)-Dimethoate in Laying Hens Following Oral Administration for 7 Consecutive Days: Lab Project Number: 761E/412W: 761E/412W-1. Unpublished study prepared by PTRL East, Inc. and PTRL West, Inc. 318 p.

Agency Review of Study: D213956, B. Cropp-Kohlligian, 04/30/96.

Study Summary: Three groups, consisting of five hens each, were orally dosed once a day for 7 consecutive days with [^{14}C-methoxy]dimethoate at a dose equivalent to 10 ppm in the feed. This dose level represents ca. 19x the maximum theoretical dietary burden for poultry. Solvent extraction and hydrolyses released 57.5-102.4% of the TRR from eggs and tissues. HPLC analyses of solubilized residues identified dimethoate carboxylic acid in egg whites (0.003 ppm, 2.4%TRR) and liver (0.131 ppm, 15.9% TRR), and omethoate in egg whites (0.006 ppm, 4.7% TRR) and liver (0.081 ppm, 9.9% TRR). However, confirmation of these metabolites by a second method was unsuccessful due to matrix interferences. Additional HPLC analyses of benzyl-derivatized ^{14}C-residues from liver indicated that simple anionic metabolites, such as dimethyl thiophosphate and dimethyl phosphate, potentially comprise only a minor portion (<10%) of the TRR in tissues. Based in indirect evidence the registrant concluded that the majority of radioactivity in poultry tissues and eggs result from incorporation of the ^{14}C-dimethyl phosphate group from dimethoate into natural products such as proteins and lipids.

Table 4. Summary of maximum dimethoate residues of concern found tissue and egg samples from the hen metabolism study. Represents ca. 19x the maximum theoretical dietary burden for poultry.

Commodity	Dimethoate	Omethoate	Dimethoate Carboxylic Acid
Liver	nd	9.9%TRR (0.081 ppm)	15.9%TRR (0.131 ppm)
Kidney	nd	nd	nd
Muscle	nd	nd	nd
Fat	nd	nd	nd
Egg Yolk	nd	nd	nd
Egg White	nd	4.7% (0.006 ppm)	2.4% (0.003 ppm)

nd = <1%TRR; <0.01 ppm

2. Feeding Study - dimethoate and omethoate fed

Study Citation: **00077495** American Cyanamid Company (1969) [Residue Study of Cygon Dimethoate and Dimethoxon in Poultry]: Report No. C-201. Includes undated methods entitled: Gas liquid chromatographic procedure for the determination of Cygon dimethoate and dimethoxon in chicken muscle and fat; Gas liquid chromatographic procedure for the determination of Cygon dimethoate and dimethoxon in eggs.

Agency Review of Study: Residue Chemistry Chapter of the Dimethoate Registration Standard dated 09/30/82

Study Summary: Residues of dimethoate and omethoate were not detected (<0.02 ppm, each compound) in liver, kidney, muscle, and fat of laying hens maintained for 21 days on a diet containing up to 1 ppm dimethoate and 0.1 ppm omethoate (ca. 2x the maximum theoretical dietary burden for poultry). Eggs collected on the last day of treatment contained no detectable residue (<0.02 ppm) of either compound.

D. Estimated Maximum Residue Levels in Meat, Milk, Poultry, and Eggs

Ruminant Tissues and Milk

Table 5. Estimated Maximum Residue Levels in Ruminant Tissues and Milk Resulting from the (1x) Maximum Theoretical Dietary Burden for Dairy Cattle.

Commodity	Goat Metabolism Study MRID 43583302 Test subjects fed [^{14}C-methoxy]dimethoate			Cattle Feeding Study MRID 00073444 Test subjects fed dimethoate and omethoate		
	Dimethoate (ppm)	Omethoate (ppm)	Dimethoate Carboxylic Acid (ppm)	Dimethoate (ppm)	Omethoate (ppm)	Dimethoate Carboxylic Acid (ppm)
Liver	<0.002	0.02	0.006	<0.01	<0.01	NR
Kidney		<0.002	<0.002		<0.01	
Muscle		<0.002	<0.002		<0.01	
Fat		<0.002	<0.002		<0.01	
Milk		<0.002	0.004		0.02	

NR = Not Reported

Poultry Tissues and Eggs

Table 6. Estimated Maximum Residue Levels in Poultry Tissues and Eggs Resulting from the (1x) Maximum Theoretical Dietary Burden for Poultry.

Commodity	Hen Metabolism Study MRID 43583301 Test subjects fed [^{14}C-methoxy]dimethoate			Hen Feeding Study MRID 00077495 Test subjects fed dimethoate and omethoate		
	Dimethoate (ppm)	Omethoate (ppm)	Dimethoate Carboxylic Acid (ppm)	Dimethoate (ppm)	Omethoate (ppm)	Dimethoate Carboxylic Acid (ppm)
Liver	<0.001	0.004	0.007	<0.01	<0.01	NR
Kidney		<0.001	<0.001			
Muscle		<0.001	<0.001			
Fat		<0.001	<0.001			
Eggs		<0.001	<0.001			

NR = Not Reported

Attachment: Chemical Structures of Dimethoate Residues of Concern (Not Available Electronically)

cc w/Attachment: B. Cropp-Kohlligian (HED/RRB4), Dimethoate Reg. Std. File, RF.
RDI: S. Hummel (06/25/02) ChemSAC (06/25/02)
7509C:RRB4:BLCKohlligian:CM#2:Rm 712N:703-305-7462:06/24/02.